

## **REMARKS**

In the Office Action dated February 25, 2005, Claims 8-29 and 37-40 are pending. The Examiner has made the restriction requirement final. Thus, Claims 19-29 and 37-40 are withdrawn from further consideration as directed to non-elected subject matter. Claim 15 is withdrawn from further consideration as directed to a non-elected species. Claims 8-14 and 16-18 which read on the elected invention are under consideration on the merits. Applicants reserve the right to file one or more divisional applications to pursue the non-elected subject matter.

This Response addresses each of the Examiner's rejections. Applicants therefore respectfully submit that the present application is in condition for allowance. Favorable consideration of all pending claims is therefore respectfully requested.

In the first instance, Applicants cancel Claims 8-14, without prejudice, in an effort to favorably advance the prosecution. Applicants reserve the right to file a continuation application to pursue the subject matter encompassed by Claims 8-14.

Claims 8-14 and 16-18 are rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite and incomplete.

Specifically, the Examiner states that Claims 8 and 16 recite methods "assaying reactivity comprising...determining reactivity by an appropriate assay." The Examiner alleges that the methods recited in Claims 8 and 16 are circular methods comprising no actual steps for which the metes and bounds of the claims can be established. The Examiner also alleges that the term "reactivity" is not defined in the specification. The Examiner further alleges that Claims 8 and 16 omit essential steps and that such omission amounts to a gap between the steps.

In response, Applicants amend Claim 16 to clarify the language and the steps of the methods. Support for the amendments to Claim 16 can be found, for example, on page 9,

lines 10 to page 10, line 19 and original Claims 8 and 16. No new matter is introduced.

Applicants also respectfully submit that the word "reactivity," although not literally defined in the specification, is clearly understood by one skilled in the art to be the quality or state of being immunoreactive or interacting immunologically. See, e.g., page 1, lines 5-10 and page 9, lines 10 to page 10, line 19. Thus, the meaning of the word "reactivity" is clear and definite in the present application.

The Examiner also indicates certain typographical errors in Claims 8 and 16. Specifically, the Examiner states that in Claim 8, "peptid3e" should be "peptide", and in Claim 16, "DDM" would properly be "IDDM." Applicants submit that the amended Claim 16 has corrected the misspelling indicated by the Examiner.

In view of the foregoing and the cancellation of Claims 8-14, Applicants respectfully submit that the rejection of Claims 8-14 and 16-18 under 35 U.S.C. §112, second paragraph, is overcome and withdrawal thereof is respectfully requested.

Claims 8-14 and 16-18 are rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking descriptive support.

The Examiner alleges that there is insufficient written description with respect to the recited "chemical equivalents" or "derivatives" of the claimed peptides. While acknowledging that the specification discloses two naturally occurring peptides, the Examiner alleges that the terms "chemical equivalents" and "derivative chemical equivalents" are not defined or exemplified.

In an effort to favorably advance the prosecution, Applicants have deleted the recitation of "chemical equivalents," "derivatives" and "derivative chemical equivalents" in the claims. However, Applicants reserve the right to file a continuation application to pursue the broader scope of the claims.

Further in view of the cancellation of Claims 8-14, the rejection of Claims 8-14 and 16-18 under 35 U.S.C. §112, first paragraph, is overcome and withdrawal thereof is respectfully requested.

Claims 8-14 and 16-18 are rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking enabling support with respect to "chemical equivalents", peptide "derivatives", or "derivative chemical equivalents." Applicants respectfully submit that the claims, as amended, no longer recite these terms. Thus, the rejection of Claims 8-14 and 16-18 under 35 U.S.C. §112, first paragraph, is overcome and withdrawal thereof is respectfully requested.

Claims 8-13 and 16-18 have been rejected under 35 U.S.C. §102(e) as allegedly anticipated by U.S. Patent No. 5,674,978 ("the '978 patent").

The Examiner is of the opinion that the '978 patent teaches a method of assaying the reactivity of a subject to IDDM autoantigen by determining the reactivity of a derivative of a peptide ( $X_1X_2X_3$ ) comprising 10 to 50, or 10 to 30, or 10 to 15 amino acid residues, wherein  $X_2$  is SEQ ID NO: 1, and wherein the peptide is capable of reacting with T cells and modifying their function in a T cell proliferation assay and the T cells are from subjects having preclinical or clinical IDDM. The Examiner particularly refers to Examples 4, 5 and 8 as well as Table 11 of the '978 patent.

Applicants observe that the '978 patent relates to GAD<sub>65</sub> polypeptides and methods of using these peptides for diagnosing and treating autoimmune diseases including

IDDM. The '978 patent discloses the amino acid sequence of the full length and certain fragments of the human GAD<sub>65</sub> polypeptides, including the 38 amino acid fragments of GAD<sub>65</sub> listed on Table 11. Applicants also observe that SEQ ID NO: 1 of the present application represents amino acid residues 24-36 of the human proinsulin polypeptide. None of the sequences disclosed in the '978 patent teaches a peptide (X<sub>1</sub>X<sub>2</sub>X<sub>3</sub>) comprising 10 to 50, or 10 to 30, or 10 to 15 amino acid residues, wherein X<sub>2</sub> is SEQ ID NO: 1. Notably, the Examiner in the Action also admits that "the use of the claimed peptide wherein X<sub>2</sub> is SEQ ID NO: 1 appears to be free of the prior art." See the Official Action on page 6, Item 12.

However, Applicants believe that the Examiner may have intended to refer to SEQ ID NO: 2, which represents amino residues 506-518 of human GAD<sub>65</sub>. In this regard, Applicants respectfully submit that the claims, as amended, do not refer to SEQ ID NO: 2. However, Applicants reserve right to file a continuation application to pursue the claims where X<sub>2</sub> is FWYIPPSLRTLED (SEQ ID NO: 2) or FWYIPQSLRGVPD (SEQ ID NO: 6).

Accordingly, the rejection of Claims 8-13 and 16-18 under 35 U.S.C. §102(e) as allegedly anticipated by the '978 patent is overcome and withdrawal thereof is respectfully requested.

Claims 8-13 and 16-18 are rejected under 35 U.S.C. §102(e) as allegedly anticipated by Miyazaki et al.

The Examiner alleges that the cited art teaches a method of assaying the reactivity of a subject to IDDM autoantigen. The Examiner alleges that the method comprises determining the reactivity of a derivative of a peptide comprising 10 to 50, or 10 to 30, or 10 to 15 amino acid residues, wherein X<sub>2</sub> (of the peptide) is SEQ ID NO: 1, and wherein the peptide is capable of reacting with T cells and modifying their function in a T cell proliferation assay and the T cells

are from subjects having clinical IDDM. The Examiner specifically refers to the "Materials and Methods: T cell Proliferation" and Table II in the Miyazaki et al. reference.

In the first instance, Applicants observe that the reference to Miyazaki et al. is a literature reference. Applicants respectfully submit that a reference under 35 U.S.C. § 102(e) must be a published patent or patent application. Thus, Applicants submit that the reference to Miyazaki et al., by definition, is not qualified as a reference under 35 U.S.C. § 102(e).

However, even assuming that the Examiner may have intended to cite the reference under 35 U.S.C. § 102(a), Applicants observe that no sequence, or any part of any sequence, in the Miyazaki et al. reference is identical to SEQ ID NO: 1. Additionally, the Examiner appears to assume that the peptide disclosed in the reference has a formula of  $X_1X_2X_3$ . However, Applicants respectfully submit that the Miyazaki et al. reference fails to support the Examiner's assumption.

Accordingly, Applicants respectfully submit that the reference to Miyazaki et al. is improper under 35 U.S.C. § 102. Therefore, the rejection of Claims 8-13 and 16-18 under 35 U.S.C. § 102(e) as allegedly anticipated by Miyazaki et al. is overcome and withdrawal thereof is respectfully requested.

The Examiner asserts that Form 1449 has not been found in the file. Applicants have enclosed a courtesy copy of Form 1449 herein which has been filed on July 26, 2005 in response to a Notice under 37 C.F.R. § 1.251 dated May 19, 2005.

In view of the foregoing amendments and remarks, it is firmly believed that the subject application is in condition for allowance, which action is earnestly solicited.

Respectfully submitted,

A handwritten signature in black ink, appearing to read 'Frank S. DiGiglio', written over the printed name.

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